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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,845	10/18/2001	Fred Levine	023070-110910US	7736

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EXAMINER

LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
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1636

10

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/041,845

Applicant(s)

LEVINE ET AL.

Examiner

David A. Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 July 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 11 and 22-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-21 and 31-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-10, 12-21 and 31-35) in Paper No. 8 is acknowledged. The traversal is on the ground(s) that it would not be an undue search burden for the examiner to search all of the claims, and that the examiner has failed to show the required search burden. This is not found persuasive because the examiner has established a search burden for the different inventions by indicating that the different inventive Groups are classified in different classes/subclasses.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-35 are pending in the instant application. Claims 11 and 22-30 are withdrawn as being drawn to a non-elected invention with traverse. Claims 1-10, 12-21 and 31-35 are ready for examination in the instant application.

Priority

Applicant has indicated in the first line of the instant specification that the present application is "related" to US Patent Application No. 09/522,376 (henceforth the '376 application). It is unclear if this is a claim for priority to the application because the nature of the relationship between the two applications (continuation, divisional, CIP) is not properly set forth in the statement. Furthermore, there is no indication in either the Official USPTO records (i.e., PALM databases), the Oath/Declaration or an Application Data Sheet indicating a desire to claim priority to the '376 application. If applicant wishes to claim priority to this application, it must be done in the proper format (see below). If applicant does not wish to claim priority to this

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application, the statement must be removed. Because it is unclear if this is an actual claim to priority under 35 USC 120, no claim to priority is acknowledged and the priority date for the instant application is indicated as the filing date of the instant application, that being October 18, 2001.

It is noted that this application appears to claim subject matter disclosed in prior Application No. 09/522,376, filed March 10, 2000. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii).

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This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Information Disclosure Statement

The information disclosure statement filed December 24, 2002 as Paper No. 6 has been considered, and a signed and initialed copy of the form PTO-1449 is attached to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 10 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the specific β lox5 cells are required to practice the invention. As such, the specific β lox5 cells must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the cells. In the instant case, the process to generate the specific β lox5 cells that is disclosed in the specification does not appear to be repeatable, nor does it appear the specific β lox5 cells are readily available to the public.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

- a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;
- b) all restrictions upon availability to the public will be irrevocably removed upon the granting of the patent;
- c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request for the enforceable life of the patent, whichever is longer;
- d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and

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e) the deposit will be replaced if it should ever become inviable.

Failure to make one of the preceding indications in response to this Office Action will result in the rejection being maintained in either a second Non-Final or a Final rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Prior to setting forth the rejection under 35 USC 102(b), the Examiner wishes to clarify the interpretation of a limitation in the claim. Specifically, the claim recites the limitation “under conditions such that the β -cells are in contact with other cells in the culture.” The instant specification provides an explicit definition of these conditions on page 14, lines 18-24, indicating that such conditions simply refer to any conditions where many but not all cells are in contact with one or more cells. On pages 8 (line 30) to 10 (line 15), the specification indicates some examples of specific conditions that encompass the limitation “under conditions such that the β -cells are in contact with other cells in the culture.” These conditions include: (1) growing cells in suspension such that they form three dimensional aggregates, such as on a plate coated with a hydrogel that prevents the cells from adhering to the bottom of a dish; (2) growing cells in an incubator typically set to 37 degrees Celsius; (3) under constituents where the CO₂ concentration is between 1-10%, and preferably 5%; (4) growing cells in DME, RPMI, 1640, DMEM Iscove’s complete or McCoy’s Medium; and (5) including a 5-20% solution of human,

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horse, calf or bovine fetal serum. Thus, any conditions that meet these specific requirements will be considered to meet the limitation of “under conditions such that the β -cells are in contact with other cells in the culture.”

Claims 1-6, 12-17 and 31-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Egan *et al.* (WO 00/09666; IDS reference #14; see entire document; henceforth Egan).

Egan teaches a population of insulin secreting cells and using the cells to produce insulin (see for example the Abstract and page 18, lines 4-10). Specifically, the cells can be simultaneously transfected with two nucleic acids, such as those encoding IDX-1 as well as NeuroD/BETA2 (see for example page 22, lines 11-15). Egan further teaches (by reference to the prior art) that GLP-1 is known to have a powerful insulin-secreting effect on β -cells by increasing insulin biosynthesis (see for example page 4, lines 5-9). The IDX-1 and NeuroD/BETA2 expressing cells taught by Egan are then contacted with a growth factor, including GLP-1, Exendin-4, or a similar growth factor (i.e., a GLP-1 analog), resulting in the increased production of insulin (see for example page 22, lines 11-25). The culture conditions for these cells include growing the cells in DMEM media supplemented with 10% fetal calf serum, grown on 12-well cluster plates (which are known to comprise a hydrogel to prevent cells from adhering to the dish, instead causing them to grow in suspension) at 37 degrees Celsius in the presence of 5% CO₂ (see for example page 43, lines 9-17), thus the cells are grown under conditions that promote cell-to-cell contact and aggregation. Finally, Egan teaches that these cells can be used for cell therapy purposes (see for example the Abstract, last line, and page 22, line 28 to page 23, line 24). Thus, Egan anticipates claims 1-6, 12-17 and 31-32 of the instant application by teaching all of the claimed elements.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 7, 8, 18, 19, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Egan as applied in the rejection of claims 1, 12, and 31 (as well as claims 2-6, 13-17 and 32) under 35 U.S.C. § 102(b) in view of Levine *et al.* (US Patent 5,723,333; IDS reference #6; see entire document; henceforth Levine).

Egan teaches each of the elements as set forth in the rejection of claims 1, 12, and 31 (as well as claims 2-6, 13-17 and 32) under 35 U.S.C. § 102(b). However, Egan does not specifically teach the expression of one or more recombinant oncogenes in β -cells.

Levine teaches the expression of one or more oncogenes in endocrine pancreas cells, preferably those that can secrete insulin (see for example the Abstract and column 4, lines 35-42). The expression of these genes is manipulated through expression vectors having genetic elements for the excision of the oncogenic elements (i.e., the cessation of their expression) or inducible promoters operably linked to the oncogenic elements to control their expression (see for example column 4, lines 2-16). Levine also teaches that the expression of oncogenes in the cells offers the advantage of producing cell lines with an extended lifespan *in vitro*. These cells can also be used for therapeutic purposes, such as transplantation (see for example the Abstract, last line, and column 4, lines 17-34).

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It would have been obvious to the ordinary skilled artisan to combine the teachings of Egan and Levine because both teachings regard the use of pancreatic cells for the expression of insulin, and the use of these cells for therapeutic purposes. Motivation for the ordinary skilled artisan to combine these teachings comes from Levine, who indicates that the expression of one or more oncogenes in endocrine pancreatic cells increases their lifespan (and thus their ability to produce more insulin) *in vitro*; thus, the longer the cells survive, the longer they are able to produce insulin.

Absent evidence to the contrary and given the teachings of the stated prior art and the high level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 9, 20 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Egan in view of Levine as applied in the rejection of claims 7, 8, 18, 19, 33 and 34 under 35 U.S.C. § 103(a), in further view of Baetge *et al.* (US 6,358,739; see entire document; henceforth Baetge).

Egan in view of Levine teaches the same elements as indicated in the rejection of claims 7, 8, 18, 19, 33 and 34 under 35 U.S.C. § 103(a). However, neither Levine nor Egan suggests the expression of telomerase as opposed to an oncogene in order to extend the lifespan of a pancreatic β -cell.

Baetge teaches the use of telomerase to extend the lifespan of human cells (see for example the Abstract and column 2, lines 15-30). Baetge also teaches that the use of telomerase is particularly advantageous for the conditional immortalization of human primary cells, such as

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pancreatic beta cells (see for example column 4, lines 6-8). Furthermore, Baetge teaches that the use of telomerase is advantageous over the use of oncogenes for the immortalization of cells because telomerase expression does not necessarily result in a malignant transformation of cells or a loss of genetic stability in cells (see for example column 13, lines 29-53).

It would have been obvious to the ordinary skilled artisan to combine the teachings of Egan and Levine with those of Baetge because both teachings regard the immortalization of β -cells to improve their lifespan, and the use of these cells for therapeutic purposes. The motivation to combine the teachings and substitute the expression of telomerase for the expression of an oncogene comes from Baetge who teaches that telomerase does not necessarily result in a malignant transformation of cells or a loss of genetic stability in cells, as might an oncogene; this is particularly advantageous when considering the treatment aspect of each of the teachings, where it would be undesirable to treat a patient with cells that had the potential to become malignant.

Absent evidence to the contrary and given the teachings of the stated prior art and the high level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

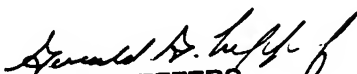
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
AU 1636


GERRY LEFFERS
PRIMARY EXAMINER